Amendments to the Specification

On page 21, after line 28, kindly insert the following table:

Table 1: Patient Demographics. Student's t-test was performed for comparison of BMI between the two groups. Kruskall-Wallis test was used for age and parity comparisons.

	Average SUI	**Average Control**	**P-value**
Age	46.6	45.8	0.9037
Parity	2.2	1.2	0.7090
Body Mass Index	27.12805	23.67377	0.18989

Kindly replace the paragraph beginning on page 21, line 29, with the following amended paragraph:

Of the 90 candidate genes identified in this study ~~identified~~ as differentially expressed with a p value assessed by two independent methods as <0.05, 62 were up-regulated and 28 were down-regulated (Table 2). The average fold increase in the up-regulated genes from SUI women compared to controls ranged from 1.3 to 4.8, while that of the down-regulated genes ranged from 1.2 to 3.1-fold.

On page 21, after line 33, kindly insert the following table:

Table 2.

1. PROBE SET*	2. GENE	3. P	4. AVG FC **
Down-regulated			
M80254	peptidylprolyl isomerase F (cyclophilin F)	0.02358	-3.1
M62982	arachidonate 12-lipoxygenase	0.03810	-2.7
Y10032	serum/glucocorticoid regulated kinase	0.01507	-2.5
X59770	type II interleukin-1 receptor, (cell line CB23)	0.00470	-2.5
U41745	PDGFA associated protein 1	0.01296	-1.8
U07806	topoisomerase (DNA) I	0.01933	-1.7
M84526	D component of complement (adipsin)	0.02513	-1.6
D31888	REST corepressor	0.00620	-1.6
U40714	tyrosyl-tRNA synthetase	0.03315	-1.6
L76465	hydroxyprostaglandin dehydrogenase 15-(NAD)	0.03121	-1.6
M91669	collagen, type XVII, alpha 1	0.03198	-1.6
M86400	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, zeta polypeptide	0.01924	-1.6

1 . PROBE SET*	2. GENE	3. P	4. AVG FC **
M86752	stress-induced-phosphoprotein 1 (Hsp70/Hsp90-organizing protein)	0.02802	-1.6
U88964	interferon stimulated gene (20kD)	0.03022	-1.5
AB002382	catenin (cadherin-associated protein), delta 1	0.03999	-1.5
D64109	transducer of ERBB2, 2	0.02597	-1.5
U28386	karyopherin alpha 2 (RAG cohort 1, importin alpha 1)	0.02849	-1.5
D13748	eukaryotic translation initiation factor 4A. Isoform 1	0.02928	-1.5
L34155	laminin, alpha 3 (nicein (l50kD), kalinin (165kD), BM600 (l50kD), epilegrin)	0.02492	-1.5
U90902	Human clone 23612 mRNA sequence	0.00296	-1.4
X52882	t-complex 1	0.03222	-1.4
X03484	v-raf-1 murine leukemia viral oncogene homolog 1	0.04554	-1.4
D86971	KIAA02I7 protein	0.01872	-1.4
M34344	Human platelet glycoprotein lib (GPllb)	0.04948	-1.4
U16660	enoyl Coenzyme A hydratase 1, peroxisomal	0.01058	-1.4
X74801	chaperonin containing TCP1, subunit 3 (gamma)	0.00586	-1.3
X94754	methionine-tRNA synthetase	0.04345	-1.3
D10522	myristoylated alanine-rich protein kinase C substrate	0.04773	-1.2
Up-regulated			
Y09306	protein kinase, Dyrk6	0.03898	4.8
U21128	Lumican	0.01996	2.7
X65724	ORF1 and ORF2 from chromosome X	0.00131	2.6
U5791I	chromosome 11 open reading frame 8	0.00508	2.5
X65962	H.sapiens mRNA for cytochrome P-450	0.04699	2.5
J02874	fatty acid binding protein 4, adipocyte	0.01939	2.4
D42108	phospholipase C-like 1	0.01651	2.3
Z11793	selenoprotein P, plasma, 1	0.00971	2.2
U60060	fasciculation and elongation protein zeta 1 (zygin l)	0.02152	2.2
J00212	leukocyte interferon (ifn-alpha) alpha-f	0.01546	2.1
AC000061	Human BAC clone	0.0046	1.9
Z18956	solute carrier famIly 6 (neurotransmitter transporter, taurine), member 6	0.01329	1.9
M73720	mast cell carboxypeptidase A (MC-CPA)	0.03110	1.9
D50930	KIAA0I40 gene product	0.01958	1.9
U49957	LIM domain containing preferred translocation partner in lipoma	0.01070	1.9
U37139	integrin beta 3 binding protein (beta3-endonexin)	0.00499	1.8
J03241	transforming growth factor, beta 3	0.01629	1.7
HG2810-HT2921	Decorin, Alt. Splice 1	0.04932	1.7
U84011	amylo-1, 6-glucosidase, 4-aipha-glucanotransferase (glycogen debranching enzyme, glycogen storage disease type III)	0.00089	1.6
D26129	KIAA0103	0.00594	1.6
L19161	eukaryotic translation initiation factor 2, subunit 3 (gamma, 52kD)	0.03920	1.6
D00726	ferrochelatase (protoporphyria)	0.01191	1.6

1. PROBE SET*	2. GENE	3. P	4. AVG FC **
D84110	RNA-binding protein gene with multiple splicing	0.01671	1.6
U94586	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 4 (9kD, MLRQ)	0.01031	1.5
U68018	MAD, mothers against decapentaplegic homolog 2 (Drosophila)	0.02684	1.5
L77730	A3 adenosine receptor (ADORA3)	0.01527	1.5
HG3431-HT3616	Hepatocyte Growth Factor Receptor	0.00112	1.5
X61970	proteasome (prosome, macropain) subunit, alpha type, 5	0.00477	1.5
D64142	H1 histone family, member X	0.00173	1.5
M15353	eukaryotic translation initiation factor 4E	0.00707	1.5
U11791	cyclin H	0.03968	1.5
U72511	repressor of estrogen receptor activity	0.04686	1.4
U76010	solute carrier family 30 (zinc transporter), member 3	0.00433	1.4
M36284	glycophorin C (Gerbich blood group)	0.01483	1.4
U90911	Human clone 23652	0.00530	1.4
L38951	karyopherin (importin) beta 1	0.01715	1.4
M22490	bone morphogenetic protein 4	0.01092	1.4
X03934	T-cell antigen receptor	0.03990	1.4
D26068	Williams-Beuren syndrome chromosome region 1	0.00153	1.4
U87408	PTH-responsive osteosarcoma B1 protein	0.04826	1.4
X82895	membrane protein, palmitoylated 2 (MAGUK p55 subfamily member 2)	0.03267	1.4
U60061	fasciculation and elongation protein zeta 2 (zygin II)	0.04455	1.4
L32832	AT-binding transcription factor 1	0.00036	1.4
M28713	NADH-cytochrome b5 reductase (b5R)	0.04908	1.4
X73478	protein phosphatase 2A, regulatory subunit B' (PR 53)	0.02267	1.4
M96803	spectrin, beta, non-erythrocytic 1	0.03801	1.4
D14659	K1AA0103 gene product	0.00453	1.4
X57206	inositol 1,4,5-trisphosphate 3-kinase B	0.04203	1.4
U56417	1-acylglycerol-3-phosphate 0-acyltransferase 1 (lysophosphatidic acid acyltransferase, alpha)	0.01957	1.4
HG2325-HT2421	Werner syndrome-1/type 4	0.03706	1.3
S81419	dystrophin {Purkinje promoter, alternatively spliced}	0.00547	1.3
HG4272-HT4542	Homeotic Protein P12	0.02034	1.3
HG114O-HT4817	Histone H1x	0.02805	1.3
D28476	thyroid hormone receptor interactor 12	0.03613	1.3
U97105	dihydropyrimidinase-like 2	0.03771	1.3
U90915	cytochrome c oxidase subunit IV isoform 1	0.02579	1.3
U37022	cyclin-dependent kinase 4 (CDK4)	0.03325	1.3
U52077	mariner1 transposase	0.03880	1.3
L43575	clone 48A8	0.02301	1.3
X80763	5-HT2c receptor	0.04036	1.3
U18300	damage-specific DNA binding protein 2 (48kD)	0.01998	1.3
U68105	poly(A)-binding protein (PABP)	0.03264	1.3

On page 22, after Table 2, kindly insert the following paragraph:

> *probe set denotes GenBank accession number
>
> ** AFC: Average fold change compares mRNA quantity in SUI to mRNA quantity in matched control. Negative fold changes indicate mRNA quantities that are lower in SUI than control. Positive-fold changes indicate mRNA quantities that are higher in SUI than control.

Kindly replace the paragraph beginning on page 24, line 22, with the following amended paragraph:

The identification of increased expression of elafin and keratin 16, both involved in the hyperproliferative response, points to altered cellular responses in pelvic tissues from women with SUI. Furthermore, elastin metabolism is implicated since elafin is a serine protease inhibitor involved in the elastin degradation pathway. A decrease in the serine protease inhibitor alpha-1 antitrypsin mRNA and protein expression in vaginal tissues from women with SUI compared to controls in the proliferative phase of the menstrual cycle was also documented in our studies. These results suggest that both collagen and elastin metabolism may be altered in women with SUI/pelvic floor dysfunction and that differential activation of genes involved in these pathways is hormone-dependent. Currently there is only one other published study that used microarray-based technology to investigate pelvic floor dysfunction. Visco et al. (*Am. J. Obstet. Gynecol.* 2003, 189:102-112) examined gene expression in pelvic muscle (pubococcygeus~~)~~ muscle) in postmenopausal women with prolapse (stage III or IV) and in control subjects without prolapse and observed differential expression of genes involved in muscle and ECM metabolism.

Kindly replace the paragraph beginning at page 27, line 10, with the following amended paragraph:

GeneChip® 5.0 Software (Affymetrix, Inc.) was used to analyze the scanned images and to obtain probe usage and quantitative information. Data were filtered to remove from further analysis probe sets (PM, perfect match; MM, mismatch) that were not detectable in all of the samples. The images were analyzed to determine an intensity value for each probe set within each gene represented on the array. The MAS 5 default algorithm (Affymetrix Microarray suite 5.1©) defines an average difference for each probe set on each array using a $\log_2$ transformed probe intensities to correct for nonspecific binding. For analysis of data generated with U133A arrays, in addition to the MAS 5 algorithm, we used the Robust Multiarray Average (RMA) algorithm developed by Rafael Irizarray (Department of Biostatistics, Johns Hopkins University) for background correction and quantile normalization for normalizing the probe intensities from different arrays to the same distribution. An R package with these algorithms is available for downloading from the Bioconductor project Web site ~~at www.bioconductor.org~~.

Kindly replace the paragraph beginning at page 28, line 28, with the following amended paragraph:

Specific sequences of oligonucleotide primers for TIMP-l, estrogen receptor-a , elafin, IL-1 ra and RAMP-1 were obtained from Gene Bank Database of the National Center for Biotechnology Information (NCBI) of the National Institutes of Health ~~(at www.2.ncbi.nlm.nih.gov/cgi-bin/genbank)~~. Corresponding sets of primers were found with the help of the program OLIGO 5.0 Primer Analysis Software (National Bioscience, Plymouth, MN) and were synthesized by the "protein, aminoacid and nucleic acid-(PAN) facility," Beckman Center, Stanford University, Stanford, CA. 'The human β-actin primers that were used to amplify an external standard were obtained from Clontech Laboratories Inc., Palo Alto, CA. β-actin mRNA expression was employed as an external positive control, being detected in all the samples studied, thus confirming the integrity of the RNA and the RT –PCR process.